

Year	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100
1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	

Field of Invention This application claims benefit under 35 U.S.C. Section 119(e) to US provisional application 60/159,394, filed October 14, 1999.

The present invention relates to compositions and crystals of androgen receptor ligand binding domain optionally in complex with its ligand. This invention also relates to methods of using the structure coordinates of the androgen receptor ligand binding domain /ligand complex to solve the structure of similar or homologous proteins or protein complexes. This invention also relates to methods for designing and selecting ligands that bind to the androgen receptor and methods of using such ligands.

Background of the Invention

The androgen receptor (AR) is a member of the steroid nuclear-receptor superfamily of ligand-dependent transcription factors. The binding of androgen to AR initiates the gene activation required for male sex development.

AR is an important target primarily in two drug discovery areas. In oncology drug discovery, inhibitors (antagonists or partial antagonists) of androgen receptor function are useful for treatment of anti-androgen refractory prostate cancer. In metabolic diseases drug discovery, agonists or partial agonists to the androgen receptor in muscle are useful to treat age-related diseases.

As with the other members of the steroid receptor family, AR has several functional domains including a DNA binding domain (DBD), and a 261 residue ligand-binding domain (LBD) (Mw = 30,245 Da) which contains the androgen binding site, and is responsible for switching on the androgen function.

Development of synthetic ligands that specifically bind to androgen receptors has been largely guided by trial and error method of drug design despite the importance of the androgen receptor in physiological processes and medical conditions such as prostate cancer and modulation of reproductive organ modulation. Previously, new ligands specific for androgen receptors were discovered in the absence of information on the three dimensional structure of the androgen receptor with a bound ligand. Before the present invention, researchers were